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Childhood Immunization Controversies: What Are Parents Asking?

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''Falsehood flies and the truth comes limping along after; so that when men come to be undeceived it is too late: the jest is over and the tale has had its effect.''

Jonathan Swift[1]

INTRODUCTION

Preventive care is the cornerstone of pediatrics, and vaccination represents one of the most important strategies in the prevention of disease in children.[2] The reduction in morbidity and mortality over the past century as a result of routine childhood immunizations is quite dramatic. Smallpox has been globally eradicated, while diseases such as diphtheria, polio, and congenital rubella are virtually nonexistent in North America. Other life-threatening conditions such as measles, Haemophilus influenza type b disease, and pertussis have been dramatically curtailed to the point where families no longer fear their devastating effects.

Public concern, both real and anecdotal, regarding the adverse effects of vaccines has circulated since the time of the first smallpox inoculation by Dr. Edward Jenner in 1796. In one survey, nearly 25% of parents reported their impression that children were receiving too many vaccines and felt that this could result in a *weakening* of their immune systems.[3] Parents worry about the ''pincushion effect,'' as current recommendations are for 19 injections in the first 2 years of life.[4] Certainly, one would expect that a biologic product administered universally would not be without adverse effects, but are these side effects overwhelmingly mild and transient, or can chronic disease or long-term neurodevelopmental impairment occur at an ''alarmingly high rate'' as reported in the lay press?[5–7] Over the past generation, as pediatricians have seen a marked reduction in acute invasive bacterial disease as a direct result of immunizations, certain noninfectious chronic diseases that present in infancy have attracted increased attention. ''Given the close temporal relationship between frequent immunizations and the onset of certain chronic childhood illnesses, it is not surprising that speculation and epidemiologic studies have attempted to link chronic disorders of childhood to immunizations … postulated links to the increased incidence of autism … have been particularly contentious.''[8]

This article attempts to place into perspective the concerns expressed by patients relative to the benefits of this most important public health intervention. *What are the questions that parents are asking their pediatricians?*

''Why Should I Have My Teenager Immunized Against Hepatitis B? She Certainly Will Not Be Using Intravenous Drugs or Having Premarital Sex or Anything Like That!''

Why do we immunize children to hepatitis B? First, it is important to know that children are at much greater risk of serious complications of this disease than are adults. While 10% of adults become chronic carriers of hepatitis B antigen after acute infection, 90% of infants run this risk, half of whom will develop end-stage liver disease. In the perinatal period, 70% to 90% of babies whose mothers are positive for hepatitis B antigen and surface antigen will acquire the infection from their mothers without intervention. Vaccine strategy mandates universal, immediate initiation of hepatitis B vaccination in the newborn period; strategies based on identifying high-risk mothers have not been effective due to late transmission in pregnancy and frequent suboptimal prenatal care. Hepatitis B immune globulin is also given in the newborn period if the mother is known to be a high-risk carrier. Exposure in the pediatric age range is bimodal; in addition to perinatal transmission, teens are also at increased risk due to high-risk behaviors including sex, intravenous drugs, tattooing, and piercing. Produced by recombinant DNA technology, the hepatitis B vaccine has 90% to 95% efficacy in

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preventing acquisition of this disease for at least 15 years from immunization.[9]

For those parents who are convinced that their child will not engage in high-risk behaviors, it is worth informing them that in 2008 activities such as attending school and playing sports might be considered ''high-risk behaviors.'' The assumption today is that universal precautions are taken and that children are vaccinated when they attend school; therefore, another child with hepatitis B who accidentally sustains an injury on the basketball court that results in bleeding should not be a threat to their child.

''My Neighbor's Baby Died Many Years Ago After a Diphtheria-Pertussis-Tetanus Vaccine.''

Fortunately, diphtheria and tetanus are quite uncommon today. Pertussis remains a serious threat and has a 1% mortality in early infancy. This fastidious gram-negative pleomorphic bacillus is easily transmissible in the catarrhal phase when symptoms are no more specific than those of the common cold. The presentation is also very atypical in infants and can be spread throughout day care centers with significant morbidity. Of interest, there has been a resurgence of pertussis in older adolescents and young adults. Despite the impressive reduction in pertussis, gaps in protection have become increasingly evident; specifically, in very early infancy prior to the initiation of vaccination and in early adulthood when vaccine protection begins to wane.[10] It is believed that 13% to 20% of chronic cough in young adults is due to pertussis. As a response to this resurgence, a new vaccine, Tdap (tetanus, diphtheria, acellular pertussis) is now recommended as the new ''tetanus booster'' for everyone 11 years of age and older. This replaces the old dT vaccine and provides ongoing pertussis protection.

The original whole-cell diphtheria-pertussis-tetanus (DPT) vaccine was quite controversial due to its common side effects of high fever, irritability, and occasional benign febrile seizures. Furthermore, it was implicated as a cause of sudden infant death and other serious chronic conditions. Groups such as ''DPT'' (Distraught Parents Together) formed because they feared that this vaccine caused brain damage. In response, the United Kingdom stopped administering this vaccination in the 1970s. Subsequent to this, there was an outbreak of pertussis resulting in 70 deaths, and the vaccine was reinstated. To cover the rising costs of liability insurance, the price of DPT vaccine jumped from $0.17 per dose to $11 per dose in the 1980s, and seven of the eight pharmaceutical companies manufacturing this vaccine discontinued production.[11] This controversy is much less of an issue today due to the new *acellular* pertussis vaccine, which is much less reactogenic. It was believed then and is known now that the temporal relationship between reports of sudden infant death and the onset of chronic disease following the administration of the old DPT vaccine was not causal. Children born with a predisposition for epilepsy or life-threatening metabolic diseases were bound to have their first manifestation of their underlying illness with their first catabolic event, which in infancy would be a high temperature; as many as 50% of infants would experience their first fever after their first DPT vaccine. Autopsies on children whose deaths were attributed to vaccination found that these children often had inborn errors of metabolism; thus, the fever from the vaccination at 2 months triggered, but did not cause, their underlying disease. A febrile viral illness could have had the same effect.

''It's Very Simple. There Has Been No Natural Polio in Our Country in More than 20 Years. My Doctor Had a Choice: He Could Have Given My Baby a Vaccine that Protects Against Polio and Has No Side Effects (IPV) or He Could Have Given Her a Vaccine that Could Cause Polio (OPV). He Chose the Latter, and My Baby Is Now Paralyzed … We Are Pursuing This in Court.'' (Circa Late 1990s)

One of the true tragedies of the vaccine era occurred with the Cutter Laboratories incident in 1955, in which inadvertent inclusion of live polio vaccine in the killed Salk vaccine resulted in 40,000 cases of abortive (transient) polio, 51 cases of paralytic polio, and 5 deaths, including Alton Ochsner's first grandson.[11,12] Immediate action was taken to discontinue that vaccine; however, why were known detrimental side effects of the subsequent live attenuated vaccine (OPV) tolerated for many years? Since the introduction of OPV by Dr. Sabin in the early 1960s, it was known that roughly 4 or 5 children in the United States per year would acquire vaccine-associated paralytic polio (VAPP). In the early 1960s, this was felt to be acceptable based on the superiority of the live vaccine in that it provided greater herd immunity, eliminated the carrier state, proved more cost effective, was easier to administer, and exponentially reduced transmission compared to the less effective killed vaccine (IPV). These infrequent cases of VAPP need to be considered in the context of the late 1950s prior to polio vaccination, when more than 16,000 children per year in the United States were afflicted with natural paralytic polio. As a result of this vaccine, not a single case of natural polio was reported in North America by the year 1978, which was a major public health advance. Vaccine experts

anticipated global polio eradication by the 21st century. For a number of reasons, this did not occur.[13]

In the United States in the late 1990s there was increasing mistrust of the entire vaccine program as the few children who acquired VAPP garnered sensational media and legal scrutiny. Unfortunately, as is often the case in preventive health, the thousands of parents whose children would have acquired natural polio annually in the absence of the vaccine were not able to advocate in its favor. Despite the objections of many scientists, the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention (CDC) reversed their recommendation for OPV in favor of IPV, in part to reinstate trust in the entire vaccine program.

''My Daughter Doesn't Need the Haemophilus Influenza Type B Vaccine Because She's Not in Day Care.''

This was a comment that was often heard by pediatricians in the late 1980s. Haemophilus influenza type b (Hib) was the most common cause of many serious and life-threatening diseases in children, such as epiglottitis, bacterial meningitis, and pericarditis. The mortality was 10% following meningitis, and 1 in 5 afflicted children sustained severe sensorineural hearing loss. Hib was certainly most common in day care centers, but epidemiologic studies revealed all infants were vulnerable. A vaccine effective in children 2 years and older was released in the mid-1980s. There was a significant decrease in disease; however, the highest risk group, children under age 2, remained unprotected.

A major advance in vaccine technology occurred with the introduction of the Hib ''conjugate'' vaccine, in which key Hib antigens were conjugated to a complex protein hapten to make it more immunogenic and to allow it to be started at 2 months of age.[14] This resulted in near eradication in our lifetime of a devastating illness. The incidence of invasive Hib disease has decreased by more than 99%.

''I Heard that the Rotavirus Vaccine Could Cause an Intestinal Blockage in My Baby.''

Rotavirus disease represents one of the most common causes of death worldwide due to infectious disease in children, primarily in underdeveloped countries. Four out of 5 children in the United States acquire rotavirus by age 5, many of whom will be hospitalized with severe dehydration.[15] This virus is easily spread by fecal oral transmission, with 10^{11} viral particles present per gram of stool. The initial vaccine was licensed in August 1999 and withdrawn months later due to a slight increase in the risk of intussusception in the immunized population. A new live oral attenuated vaccine was released in 2006 against the 5 reassortment strains that make up 96% of globally identified disease. It has been shown to be 90% effective for the prevention of severe disease, and there is no increased risk of intussusception.

This story is important to share with parents to demonstrate the immediate and definitive response to data from the Vaccine Adverse Event Reporting System when there is evidence of serious adverse effects from a vaccine.[16] The National Childhood Vaccine Injury Act of l986 mandates a detailed database of all reported adverse events associated with vaccines and also serves to protect providers who properly administer recommended immunizations. Rotashield was promptly removed from the market, at extraordinary cost to the manufacturer, and years passed before a new vaccine backed by rigorous safety trials, RotaTeq, was licensed.

''My Child Got the Pneumococcal Vaccine but Is Still Getting Ear Infections.''

For the past generation, the number one cause of serious bacterial infections in children has been *Streptococcus pneumoniae*. The burden of pneumococcal disease in childhood had intensified until recently due to the increasing resistance of this organism to commonly used antibiotics. This is attributed in large part to the inappropriate and excessive use of antibiotics in children, another important teaching point for parents.[17] In 2000, a conjugate pneumococcal vaccine was introduced for children 2 months of age and older that included 7 serotypes representing the most common virulent strains seen in childhood. Since that time, the incidence of invasive disease has decreased by 80% for those less than 2 years of age, including a 90% decrease in vaccine-related serotypes.[18] Otitis media continues to be a major problem for children, but parents are reminded that this vaccine was directed more toward the virulent serotypes than to the most common ones.

''Can You Give My Baby that Nasal Flu Vaccine? I Don't Want Him to Get the Shot Because I Understand It Contains Thimerosal that Could Lead to Brain Damage.''

Influenza is a very serious infection in high-risk children; the vaccine is now recommended for children 6 months and older. Next fall, it will be recommended for all children over 6 months. Traditionally, the inactivated vaccine (TIV) was administered to children, but the new live attenuated nasal mist is approved for healthy children 2 years and older and actually appears to be more efficacious.[19]

The preservative in TIV is a compound known as thimerosal, an organic ethyl mercury derivative.[20]

Unsubstantiated theories linking thimerosal to brain damage have rampantly circulated in forums ranging from Internet blogs to play groups. The fact is that infants who are exclusively breast-fed will be exposed to 15 times the mercury found in the influenza vaccine. Despite extensive studies, there are no data available to implicate thimerosal in any human disease. A recent study failed to find any causal association between early exposure to mercury from thimerosal-containing vaccines and any deficit in neuropsychological function in children 7–10 years of age.[21] Despite the lack of positive findings, thimerosal has been removed from all vaccines at this time except for some influenza vaccines, as the CDC and American Academy of Pediatrics elected to exercise the ''precautionary principle.'' This has resulted in considerable increased cost with what many believe to be an ambiguous message to the public.[22]

''I Read that Hepatitis A Is a Very Mild Disease in Children. Why Do You Immunize Against It?''

A recent recommendation[23] advocated hepatitis A vaccination for all children between 12 and 23 months of age rather than for only high-risk children. It is estimated that there were more than 300,000 cases of hepatitis A per year in the United States. The majority of cases were in children under 5, and these often went undetected due to the fact that 30% of cases are anicteric and asymptomatic. We have seen a dramatic decrease of hepatitis A in all ages in the United States since the introduction of the childhood vaccine. As with the influenza vaccine, hepatitis A immunization in children has an even greater impact on the health of adults through herd immunity.

''I'm Anxious Because My Friend Is Adamant that the Measles-Mumps-Rubella Vaccine Can Lead to Autism in Children.''

Congenital rubella, which caused severe prenatal damage to fetuses and resulted in mental retardation and other organ system failure, has become a thing of the past due to this vaccine. Mumps, though still present, is much less common than it was before this vaccine was administered, and measles, with the exception of occasional outbreaks in unvaccinated populations, is also quite rare. Prior to 1963, measles was the most contagious infection in humans. This particular virus caused 30% of all deaths due to vaccine-preventable diseases in the early 1960s. One in 1000 children who acquired measles developed acute encephalitis with the potential for permanent brain damage. Extremely rare reports of encephalitis or encephalopathy in children who had received the vaccine have been reported with an estimated incidence of less than 1 case per 1 million vaccinations.

A case in *Lancet* in 1998 linked the measles-mumps-rubella vaccine with autism.[5] The data have subsequently been shown to be flawed, and the journal and nearly all authors have retracted their initial interpretation of the findings.[24–26] The Institute of Medicine vaccine safety review, as well as other publications, have published statements ''refuting all causal relationships'' between the vaccine and autism.[27]

Parents are justified in their concerns about the rising incidence of autism in children. For pediatricians, it is striking that many of the causes of invasive bacterial disease that were so common 2 decades ago are essentially eradicated today. In their place, increased attention has been shifted to chronic conditions, primarily psychosocial and neurodevelopmental ones, such as attention deficit hyperactivity disorder and autism. In addition, the most common physical disease, obesity, a manifestation of genetic predisposition and societal trends, is resulting in rising numbers of adolescents with diabetes and hypertension. The reasons for the increase in reports of autism (now estimated to affect 1 in 150 children) can be explained in large part by the much broader definition of the autistic spectrum, ranging from children who are severely retarded with autistic features to mainstreamed, at times highly intelligent individuals who have challenges in communication skills and social nuance (such as those with Asperger's syndrome). Some scientists feel that there may well be an environmental contribution to the expression of autism; however, by all scientific research available to date, this environmental trigger does not appear to be vaccines.[28,29]

''We'll Pass. I'd Rather Have My Child Get Natural Chicken Pox so it Won't Recur in Adulthood When It Can Really Be Dangerous!''

To many parents, chicken pox is a mild illness that is a rite of passage. However, the social and financial implications of children missing a week of school and parents staying home from work is huge from a global perspective; the cost to society of varicella was estimated to be $399 million per year in the United States.[30] More importantly, we remind parents that in addition to the possibility of scarring and secondary bacterial infections, roughly 200 previously healthy children every year died from complications of chicken pox prior to licensing of the vaccine. Also, 2% of nonimmune pregnant women exposed to chicken pox before 20 weeks gestation were at risk of embryopathy that could prove fatal to their fetuses.

The annual mortality due to varicella dramatically decreased from 1990 to 2000 as a result of universal vaccination. Other concerns, such as increased rates of zoster, were proven untrue. A booster varicella vaccine was recently recommended to further reduce the risk of chicken pox in later life.[30] It was known from the onset that roughly 10% of children could develop a mild case of chicken pox after subsequent exposure due to waning titers and rare episodes of primary vaccine failure. This number seems to have increased since the initiation of this vaccine. One reason for this is the fact that varicella has become so uncommon that immunized children no longer get a ''booster effect'' when exposed to a child with active disease.

''I Thought Meningococcal Disease Was Fairly Rare. If My Insurance Doesn't Cover this Expensive Shot, I Don't Think We'll Get It.''

When asked, most pediatricians will list meningococcemia as one of the most dreaded acquired diseases of childhood. The frequent reports of college students dying of meningococcal disease are devastating to families as well as to the entire community. The highest rates of this disease occur in infants, teenagers and young adults living in barracks or dormitories, the elderly, and individuals with complement deficiencies. The mortality is 10% in all ages and 25% in teenagers. Roughly 10% of people carry the bacteria asymptomatically in the nasopharynx, and 95% of cases in the United States are sporadic. The meningococcal vaccine was released in 2005 against strains A, C, Y, and W-135 and is licensed for all individuals between ages 11 and 55.[31] It is hoped that this vaccine, which is currently undergoing age trials, will be approved down to infancy.

Fortunately, parents do not have to worry about the cost of vaccines in the United States; free vaccines are available to all uninsured and underinsured children through the Vaccines for Children program.[32] However, vaccine shortages continue to occur with worrisome frequency.[33]

''Don't You Think this Human Papillomavirus Vaccine Will Encourage My Daughter to Have Sex?''

The most common sexually transmitted disease (STD) in the United States today is human papillomavirus (HPV) infection; more than 20 million Americans are currently infected, including half of all sexually active people. Annually, 6.2 million new infections occur, with half in females under 24 years of age. Though most infections with HPV are asymptomatic and resolve with time, roughly 10% of exposures to oncogenic strains become persistent and are responsible for most cases of cervical cancer. These strains have also been found to lead to cancer of the vulva, anus, vagina, and penis; rarely, neonates born to infected mothers can develop severe recurrent respiratory papillomatosis. In 2006, the quadrivalent HPV vaccine was licensed for females between the ages of 9 and 26 years of age. The vaccine provides protection against HPV types 16 and 18, which cause more than 70% of cervical cancer cases, and types 6 and 11, which lead to more than 90% of genital warts.[34] Immunizing girls before the onset of sexual activity is key because the vaccine does not protect against disease from previously acquired HPV infection. The vaccine is certainly not intended to replace other preventive strategies.

Controversy has surrounded this vaccine, particularly as certain states attempt to mandate it. ''Opposition seems to be based on the concern that to recognize the reality of teenage sexual activity is to implicitly endorse it.''[35] When presenting this vaccination to parents, physicians should focus on the universal aspect of the recommendation, the efficacy and safety of the vaccine, and the direct link to cancer prevention. In addition to receiving this vaccination, the best preventive strategy to minimize STDs is parental supervision and ongoing communication between parents and their teenagers.

CONCLUSION

In conclusion, it is critical that physicians remain up to date on vaccine efficacy and safety and serve as advocates for timely administration. The media have aggressively focused on controversies regarding immunizations, often with little regard for science. This focus has resulted in increased parental anxiety, confusion, and, at times, refusal to vaccinate. Clearly, researchers must continue to provide data proving the absence of harm from vaccines.[36–39] Primary care physicians must remain current on all proven and perceived concerns regarding childhood immunizations and must be prepared to make the case that any small risk is dramatically outweighed by the advantages to the child and to society.

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